PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PN0353-PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/NO2004/000208	International filing date *(day/month/year)* 07.07.2004	Priority date *(day/month/year)* 08.07.2003
International Patent Classification (IPC) or national classification and IPC C07K14/705, C07K5/09, A61K38/17, A61K38/06, A61K49/00, G01N33/58, G01N33/68		
Applicant AMERSHAM HEALTH AS		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand 18.04.2005	Date of completion of this report 19.09.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Schmidt, Harald Telephone No. +31 70 340-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NO2004/000208

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-30 as originally filed

Sequence listings part of the description, Pages

31-33 as originally filed

Claims, Numbers

1-13 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-13 (all partially) and 13 (also as to IA)

because:

☒ the said international application, or the said claims Nos. 13 (as to IA) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-13 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-9
	No:	Claims	1,10-13
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-13
Industrial applicability (IA)	Yes:	Claims	1-12
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

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Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 13 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of claim 13 (Article 34(4)(a)(I) PCT).

The scope of claims 1 to 13, in as far as the expressions "arginine mimetic" (claim 1), "derivatives" (claims 2 and 5) are concerned, is so unclear (Article 6 PCT) that a meaningful international search is impossible with regard to these expressions. Therefore, no opinion on novelty, inventive step and industrial applicability will be given with regard to said expressions.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US2002/0102217 (01 August 2002)
D2: Katada J et al. (1997) J. Biol. Chem. 272: 7720-7726
D3: DE 198 08 591 (16 September 1999)
D4: Riecke B et al. (2001) Horm. Metab. Res. 33: 307-311
D5: WO 02/26776 (04 April 2002)

Novelty

The document D1 discloses fluorescein-labeled RGD-peptides for use as therapeutic or diagnostic imaging agents (see Example 13 and claims 11,19 and 31).
Therefore, the subject-matter of claims 1 and 10 to 13 does not meet the requirements of Article 33(2) PCT.

The document D2 discloses fluorescein-labeled RGD-peptides for use in flow cytometric studies (see abstract and Figure 2).
Therefore, the subject-matter of claims 1 and 10 does not meet the requirements of Article 33(2) PCT.

The document D3 discloses fluorescein-labeled RGD-peptides for use in flow cytometric assays (see column 3, line 20 - line 30).
Therefore, the subject-matter of claims 1 and 10 does not meet the requirements of Article 33(2) PCT.

The document D4 discloses an cyclo-RGD peptide linked to N-(fluorescein-6-carboxy-) lysine that is able to permeate the cornea (see page 308 and Figure 2).
Therefore, the subject-matter of claims 1 and 10 does not meet the requirements of Article 33(2) PCT.

Inventive step

The document D5 is considered to represent the closest prior art for subject-matter of claims 2 to 9 and discloses labelled peptides comprising the RGD motif and cysteine residues that allow the formation of intramolecular bounds.
It is further disclosed that fluorophores or light imaging reporter groups are useful as labeling agents (see pages 8,9,16,17,23 and the claims).

The subject-matter of claims 2 to 9 differs in that the peptides are labeled with fluorescein.

The problem to be solved resides in the provision of further compounds for use in treatment and diagnostic optical imagining of angiogenesis-related diseases.

The solution is considered to be the use of fluorescein as labeling agent.

The document D5, disclosing a wide range of labelling agents, guides the artisan to select further labels, and fluorescein-labelled RGD peptides are known from the documents D1 to D4. It would therefore appear a routine choice for the skilled person to use fluorescein-labelled RGD-containing peptides to solve the problem posed.
Hence, the subject-matter of claims 2 to 9 does not involve an inventive step in the sense off Article 33(3) PCT, unless an unexpected advantageous effect can be

demonstrated.

Industrial applicability

For the assessment of the present claim 13 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.